Regulation and with the specific provisions laid down in the relevant Community legislation. Council Directive 2001/112/EC of 20 December 2001 relating to fruit juices and certain similar products intended for human consumption [1], Council Directive 83/417/EEC of 25 July 1983 on the approximation of the laws of the Member States relating to certain lactoproteins (caseins and caseinates) intended for human consumption [2] and Council Regulation (EC) No 1493/1999 of 17 May 1999 on the common organisation of the market in wine [3] should therefore be amended accordingly. Since all food enzymes should be covered by this Regulation, Regulation (EC) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients [4] should be amended accordingly.

(8) Food enzymes the use of which is permitted within the Community should appear in a Community list that should clearly describe the enzymes and specify any conditions governing their use, including where necessary information on their function in the final food. This list should be supplemented by specifications, in particular on their origin, including where relevant information about allergenic properties, and purity criteria.

(9) In order to ensure harmonisation, the risk assessment of food enzymes and their inclusion in the Community list should be carried out in accordance with the procedure laid down in Regulation (EC) No 1331/2008 of the European Parliament and of the Council of 16 December 2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings [5].

(10) Under Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety [6], the European Food Safety Authority (hereinafter referred to as the Authority) is to be consulted on matters likely to affect public health.

(11) A food enzyme which falls within the scope of Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed [7] should be authorised in accordance with that Regulation as well as under this Regulation.

(12) A food enzyme already included in the Community list under this Regulation which is prepared by production methods or using starting materials significantly different from those included in the risk assessment of the Authority, or different from those covered by the authorisation and the specifications under this Regulation, should be submitted for evaluation by the Authority. 'Significantly different' could mean *inter alia* a change of the production method from extraction from a plant to production by fermentation using a micro-organism or a genetic modification of the original micro-organism, a change in starting materials, or a change in particle size.

(13) Since many food enzymes are already on the Community market, provision should be made to ensure that the switchover to a Community list of food enzymes takes place smoothly and does not disturb the existing food enzyme market. Sufficient time should be allowed for applicants to make available the information necessary for the risk assessment of these products. An initial two-year period should therefore be allowed following the date of application of the implementing measures to be laid down in accordance with Regulation (EC) No 1331/2008 [establishing a common authorisation procedure for food additives, food enzymes and food flavourings], in order to give applicants sufficient time to submit the information on existing enzymes which may be included in the Community list to be drawn up under this Regulation. It should also be possible to submit applications for the authorisation of new enzymes during the initial two-year period. The Authority should evaluate without delay all applications for food enzymes for which sufficient information has been submitted during that period.

(14) In order to ensure fair and equal conditions for all applicants, the Community list should be drawn up in a single step. That list should be established after completion of the risk assessment of all food enzymes for which sufficient information has been submitted during the initial two-year period. However, the risk assessments of the Authority for individual enzymes should be published as soon as they are completed.

(15) A significant number of applications is expected to be submitted during the initial two-year period. A lengthy period may therefore be needed before the risk assessment of these has been completed and the Community list is drawn up. In order to ensure equal access to the market for new food enzymes after the initial two-year period, a transitional period should be provided for during which food enzymes and food using food enzymes may be placed on the market and used, in accordance with the existing national rules in the Member States, until the Community list has been drawn up.

[1] OJ L 10, 12.1.2002, p. 58.
[2] OJ L 237, 26.8.1983, p. 25.
[3] OJ L 179, 14.7.1999, p. 1.
[4] OJ L 43, 14.2.1997, p. 1.
[5] See page 1 of this Official Journal.
[6] OJ L 31, 1.2.2002, p. 1.
[7] OJ L 268, 18.10.2003, p. 1.

(16) The food enzymes E 1103 Invertase and E 1105 Lysozyme, that have been authorised as food additives under Directive 95/2/EC of the European Parliament and of the Council of 20 February 1995 on food additives other than colours and sweeteners [1], and the conditions governing their use should be carried over from Directive 95/2/EC to the Community list when it is drawn up by this Regulation. In addition, Council Regulation (EC) No 1493/1999 authorises the use of urease, beta-glucanase and lysozyme in wine subject to the conditions laid down in Commission Regulation (EC) No 423/2008 of 8 May 2008 on laying down certain detailed rules for implementing Council Regulation (EC) No 1493/1999 and establishing a Community code of oenological practices and processes [2]. Those substances are food enzymes and they should fall within the scope of this Regulation. They should therefore also be added to the Community list when it is drawn up for their use in wine in accordance with Regulation (EC) No 1493/1999 and Regulation (EC) No 423/2008.

(17) Food enzymes remain subject to the general labelling obligations provided for in Directive 2000/13/EC of the European Parliament and of the Council of 20 March 2000 on the approximation of the laws of the Member States relating to the labelling, presentation and advertising of foodstuffs [3] and, as the case may be, in Regulation (EC) No 1829/2003 and in Regulation (EC) No 1830/2003 of the European Parliament and of the Council of 22 September 2003 concerning the traceability and labelling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms [4]. In addition, specific provisions on the labelling of food enzymes sold as such to the manufacturer or to the consumer should be contained in this Regulation.

(18) Food enzymes are covered by the definition of food in Regulation (EC) No 178/2002 and are therefore, when used in food, required to be indicated as ingredients in the labelling of the food in compliance with Directive 2000/13/EC. Food enzymes should be designated by their technological function in food, followed by the specific name of the food enzyme. However, provision should be made for a derogation from the provisions on labelling in cases where the enzyme performs no technological function in the final product but is present in the foodstuff only as a result of carry-over from one or more of the ingredients of the foodstuff or where it is used as a processing aid. Directive 2000/13/EC should be amended accordingly.

(19) Food enzymes should be kept under continuous observation and should be re-evaluated whenever necessary in the light of changing conditions governing their use and new scientific information.

(20) The measures necessary for the implementation of this Regulation should be adopted in accordance with Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission [5].

(21) In particular the Commission should be empowered to adopt appropriate transitional measures. Since those measures are of general scope and are designed to amend non-essential elements of this Regulation, *inter alia*, by supplementing it with new non-essential elements, they must be adopted in accordance with the regulatory procedure with scrutiny provided for in Article 5a of Decision 1999/468/EC.

(22) In order to develop and update Community law on food enzymes in a proportionate and effective way, it is necessary to collect data, share information and coordinate work between Member States. For that purpose, it may be useful to undertake studies to address specific issues with a view to facilitating the decision-making process. It is appropriate that the Community finance such studies as part of its budgetary procedure. The financing of such measures is covered by Regulation (EC) No 882/2004 of the European Parliament and of the Council of 29 April 2004 on official controls performed to ensure the verification of compliance with feed and food law, animal health and animal welfare rules [6].

(23) Member States are to carry out official controls in order to enforce compliance with this Regulation in accordance with Regulation (EC) No 882/2004.

(24) Since the objective of this Regulation, namely to lay down Community rules on food enzymes, cannot be sufficiently achieved by the Member States and can therefore, in the interests of market unity and a high level of consumer protection, be better achieved at Community level, the Community may adopt measures, in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty. In accordance with the principle of proportionality, as set out in that Article, this Regulation does not go beyond what is necessary in order to achieve that objective,

[1] OJ L 61, 18.3.1995, p. 1.
[2] OJ L 127, 15.5.2008, p. 13.
[3] OJ L 109, 6.5.2000, p. 29.
[4] OJ L 268, 18.10.2003, p. 24.
[5] OJ L 184, 17.7.1999, p. 23.
[6] OJ L 165, 30.4.2004, p. 1. Corrected version in OJ L 191, 28.5.2004, p. 1.

HAVE ADOPTED THIS REGULATION:

CHAPTER I

SUBJECT MATTER, SCOPE AND DEFINITIONS

Article 1

Subject matter

This Regulation lays down rules on food enzymes used in foods, including such enzymes used as processing aids, with a view to ensuring the effective functioning of the internal market whilst ensuring a high level of protection of human health and a high level of consumer protection, including the protection of consumer interests and fair practices in food trade, taking into account, where appropriate, the protection of the environment.

For those purposes, this Regulation provides for:

(a) a Community list of approved food enzymes;

(b) conditions of use of food enzymes in foods;

(c) rules on the labelling of food enzymes sold as such.

Article 2

Scope

1. This Regulation shall apply to food enzymes as defined in Article 3.

2. This Regulation shall not apply to food enzymes when and insofar as they are used in the production of:

(a) food additives falling within the scope of Regulation (EC) No 1333/2008 [on food additives];

(b) processing aids.

3. This Regulation shall apply without prejudice to any specific Community rules concerning the use of food enzymes:

(a) in specific foods;

(b) for purposes other than those covered by this Regulation.

4. This Regulation shall not apply to microbial cultures that are traditionally used in the production of food and which may incidentally produce enzymes, but which are not specifically used to produce them.

Article 3

Definitions

1. For the purposes of this Regulation, the definitions laid down in Regulation (EC) No 178/2002, Regulation (EC) No 1829/2003 and Regulation (EC) No 1333/2008 [on food additives] shall apply.

2. The following definitions shall also apply:

(a) 'food enzyme' means a product obtained from plants, animals or micro-organisms or products thereof including a product obtained by a fermentation process using micro-organisms:

(i) containing one or more enzymes capable of catalyzing a specific biochemical reaction; and

(ii) added to food for a technological purpose at any stage of the manufacturing, processing, preparation, treatment, packaging, transport or storage of foods;

(b) 'food enzyme preparation' means a formulation consisting of one or more food enzymes in which substances such as food additives and/or other food ingredients are incorporated to facilitate their storage, sale, standardisation, dilution or dissolution.

CHAPTER II

COMMUNITY LIST OF APPROVED FOOD ENZYMES

Article 4

Community list of food enzymes

Only food enzymes included in the Community list may be placed on the market as such and used in foods, in accordance with the specifications and conditions of use provided for in Article 7(2).

Article 5

Prohibition of non-compliant food enzymes and/or non-compliant food

No person shall place on the market a food enzyme or any food in which such a food enzyme has been used if the use of the food enzyme does not comply with this Regulation and its implementing measures.

Article 6

General conditions for inclusion of food enzymes in the Community list

A food enzyme may be included in the Community list only if it meets the following conditions and, where relevant, other legitimate factors:

(a) it does not, on the basis of the scientific evidence available, pose a safety concern to the health of the consumer at the level of use proposed;

(b) there is a reasonable technological need, and

(c) its use does not mislead the consumer. Misleading the consumer includes, but is not limited to, issues related to the nature, freshness and quality of the ingredients used, the naturalness of a product or of the production process, or the nutritional quality of the product.

Article 7

The content of the Community list of food enzymes

1. A food enzyme which complies with the conditions set out in Article 6 may, in accordance with the procedure referred to in Regulation (EC) No 1331/2008 [establishing a common authorisation procedure for food additives, food enzymes and food flavourings], be included in the Community list.

2. The entry of a food enzyme in the Community list shall specify:

(a) the name of the food enzyme;

(b) the specifications of the food enzyme, including its origin, purity criteria and any other necessary information;

(c) the foods to which the food enzyme may be added;

(d) the conditions under which the food enzyme may be used; where appropriate, no maximum level shall be fixed for a food enzyme. In that case, the food enzyme shall be used in accordance with the *quantum satis* principle;

(e) if appropriate, whether there are any restrictions on the sale of the food enzyme directly to the final consumer;

(f) where necessary, specific requirements in respect of the labelling of food in which the food enzymes have been used in order to ensure that the final consumer is informed of the physical condition of the food or the specific treatment it has undergone.

3. The Community list shall be amended in accordance with the procedure referred to in Regulation (EC) No 1331/2008 [establishing a common authorisation procedure for food additives, food enzymes and food flavourings].

Article 8

Food enzyme falling within the scope of Regulation (EC) No 1829/2003

1. A food enzyme falling within the scope of Regulation (EC) No 1829/2003 may be included in the Community list in accordance with this Regulation only when it is covered by an authorisation in accordance with Regulation (EC) No 1829/2003.

2. When a food enzyme already included in the Community list is produced from a different source falling within the scope of Regulation (EC) No 1829/2003, it will not require a new authorisation under this Regulation, as long as the new source is covered by an authorisation in accordance with Regulation (EC) No 1829/2003 and the food enzyme complies with the specifications established under this Regulation.

Article 9

Interpretation decisions

Where necessary, it may be decided in accordance with the regulatory procedure referred to in Article 15(2) whether or not:

(a) a given substance meets the definition of food enzyme in Article 3;

(b) a particular food belongs to a category of food in the Community list of food enzymes.

CHAPTER III

LABELLING

Article 10

Labelling of food enzymes and food enzyme preparations not intended for sale to the final consumer

1. Food enzymes and food enzyme preparations not intended for sale to the final consumer, whether sold singly or mixed with each other and/or other food ingredients, as defined in Article 6(4) of Directive 2000/13/EC, may only be marketed with the labelling provided for in Article 11 of this Regulation, which must be easily visible, clearly legible and indelible. The information provided for in Article 11 shall be in a language easily understandable to purchasers.

2. Within its own territory, the Member State in which the product is marketed may, in accordance with the Treaty, stipulate that the information provided for in Article 11 shall be given in one or more of the official languages of the Community, to be determined by that Member State. This shall not preclude such information from being indicated in several languages.

Article 11

General labelling requirements for food enzymes and food enzyme preparations not intended for sale to the final consumer

1. Where food enzymes and food enzyme preparations not intended for sale to the final consumer are sold singly or mixed with each other and/or other food ingredients, their packaging or containers shall bear the following information:

(a) the name laid down under this Regulation in respect of each food enzyme or a sales description which includes the name of each food enzyme or in the absence of such a name, the accepted name laid down in the nomenclature of the International Union of Biochemistry and Molecular Biology (IUBMB);

(b) the statement 'for food' or the statement 'restricted use in food' or a more specific reference to its intended food use;

(c) if necessary, the special conditions of storage and/or use;

(d) a mark identifying the batch or lot;

(e) instructions for use, if the omission thereof would preclude appropriate use of the food enzyme;

(f) the name or business name and address of the manufacturer, packager or seller;

(g) an indication of the maximum quantity of each component or group of components subject to quantitative limitation in food and/or appropriate information in clear and easily understandable terms enabling the purchaser to comply with this Regulation or other relevant Community law; where the same limit on quantity applies to a group of components used singly or in combination, the combined percentage may be given as a single figure; the limit on quantity shall be expressed either numerically or by the *quantum satis* principle;

(h) the net quantity;

(i) the activity of the food enzyme(s);

(j) the date of minimum durability or use-by-date;

(k) where relevant, information on a food enzyme or other substances as referred to in this Article and listed in Annex IIIa to Directive 2000/13/EC.

2. Where food enzymes and/or food enzyme preparations are sold mixed with each other and/or with other food ingredients, their packaging or containers shall bear a list of all ingredients in descending order of their percentage by weight of the total.

3. The packaging or containers of food enzyme preparations shall bear a list of all components in descending order of their percentage by weight of the total.

4. By way of derogation from paragraphs 1, 2 and 3, the information required in paragraph 1 points (e) to (g) and in paragraphs 2 and 3 may appear merely on the documents relating to the consignment which are to be supplied with or prior to the delivery, provided that the indication 'not for retail sale' appears on an easily visible part of the packaging or container of the product in question.

5. By way of derogation from paragraphs 1, 2 and 3, where food enzymes and food enzyme preparations are supplied in tankers all of the information may appear merely on the accompanying documents relating to the consignment which are to be supplied with the delivery.

Article 12

Labelling of food enzymes and food enzyme preparations intended for sale to the final consumer

1. Without prejudice to Directive 2000/13/EC, Council Directive 89/396/EEC of 14 June 1989 on indications or marks identifying the lot to which a foodstuff belongs [1] and Regulation (EC) No 1829/2003, food enzymes and food enzyme preparations sold singly or mixed with each other and/or other food ingredients intended for sale to the final consumer may be marketed only if their packaging contains the following information:

(a) the name laid down under this Regulation in respect of each food enzyme or a sales description which includes the name of each food enzyme or in the absence of such a name, the accepted name laid down in the nomenclature of the IUBMB;

[1] OJ L 186, 30.6.1989, p. 21.

(b) the statement 'for food' or the statement 'restricted use in food' or a more specific reference to its intended food use.

2. For the information provided for in paragraph 1 of this Article, Article 13(2) of Directive 2000/13/EC shall apply accordingly.

Article 13

Other labelling requirements

Articles 10 to 12 shall be without prejudice to more detailed or more extensive laws, regulations or administrative provisions regarding weights and measures or applying to the presentation, classification, packaging and labelling of dangerous substances and preparations or applying to the transport of such substances and preparations.

CHAPTER IV

PROCEDURAL PROVISIONS AND IMPLEMENTATION

Article 14

Information obligation

1. A producer or user of a food enzyme shall inform the Commission immediately of any new scientific or technical information which might affect the assessment of the safety of the food enzyme.

2. For a food enzyme already approved under this Regulation which is prepared by production methods or using starting materials significantly different from those included in the risk assessment of the European Food Safety Authority (hereinafter referred to as the Authority), a producer or user shall, before marketing the food enzyme, submit to the Commission the necessary data to allow an evaluation of the food enzyme with regard to the modified production method or characteristics to be undertaken by the Authority.

3. A producer or user of a food enzyme shall, at the request of the Commission, inform it of the actual use of the food enzyme. Such information shall be made available to Member States by the Commission.

Article 15

Committee

1. The Commission shall be assisted by the Standing Committee on the Food Chain and Animal Health.

2. Where reference is made to this paragraph, Articles 5 and 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

The period laid down in Article 5(6) of Decision 1999/468/EC shall be set at three months.

3. Where reference is made to this paragraph, Article 5a(1) to (4) and Article 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

Article 16

Community financing of harmonised policies

The legal basis for the financing of measures resulting from this Regulation shall be Article 66(1)(c) of Regulation (EC) No 882/2004.

CHAPTER V

TRANSITIONAL AND FINAL PROVISIONS

Article 17

Establishment of the Community list of food enzymes

1. The Community list of food enzymes shall be drawn up on the basis of applications made pursuant to paragraph 2.

2. Interested parties may submit applications for the inclusion of a food enzyme in the Community list.

The deadline for submitting such applications shall be 24 months after the date of application of the implementing measures to be laid down in accordance with Article 9(1) of Regulation (EC) No 1331/2008 [establishing a common authorisation procedure for food additives, food enzymes and food flavourings].

3. The Commission shall establish a Register of all food enzymes to be considered for inclusion in the Community list in respect of which an application complying with the validity criteria to be laid down in accordance with Article 9(1) of Regulation (EC) No 1331/2008 [establishing a common authorisation procedure for food additives, food enzymes and food flavourings] has been submitted in accordance with paragraph 2 of this Article (hereinafter referred to as the Register). The Register shall be made available to the public.

The Commission shall submit the applications to the Authority for its opinion.

4. The Community list shall be adopted by the Commission in accordance with the procedure laid down in Regulation (EC) No 1331/2008 [establishing a common authorisation procedure for food additives, food enzymes and food flavourings], once the Authority has issued an opinion on each food enzyme included in the Register.

However, by way of derogation from that procedure:

(a) Article 5(1) of Regulation (EC) No 1331/2008 [establishing a common authorisation procedure for food additives, food enzymes and food flavourings] shall not apply to the Authority's adoption of its opinion;

(b) the Commission shall adopt the Community list for the first time after the Authority has delivered its opinion on all the food enzymes listed in the Register.

5. If necessary, any appropriate transitional measures for the purposes of this Article which are designed to amend non-essential elements of this Regulation, *inter alia*, by supplementing it, shall be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 15(3).

Article 18

Transitional measures

1. Notwithstanding Articles 7 and 17 of this Regulation, the Community list shall, when drawn up, include the following food enzymes:

(a) E 1103 Invertase and E 1105 Lysozyme, stating the conditions governing their use as specified in Annex I and Part C of Annex III to Directive 95/2/EC;

(b) Urease, beta-glucanase and lysozyme for use in wine in accordance with Regulation (EC) No 1493/1999 and the implementing rules for that Regulation.

2. Food enzymes, food enzyme preparations and food containing food enzymes placed on the market or labelled before 20 January 2010 which do not comply with the provisions of Articles 10 to 12 may be marketed until their date of minimum durability or use-by-date.

Article 19

Amendments to Directive 83/417/EEC

In Directive 83/417/EEC, in Annex I, Section III(d), the indents shall be replaced by the following:

'— rennet meeting the requirements of Regulation (EC) No 1332/2008 of the European Parliament and of the Council of 16 December 2008 on food enzymes (*);

— other milk-coagulating enzymes meeting the requirements of Regulation (EC) No 1332/2008.

(*) OJ L 354, 31.12.2008, p. 7.'

Article 20

Amendment to Regulation (EC) No 1493/1999

In Regulation (EC) No 1493/1999, the following paragraph shall be added to Article 43:

'3. Enzymes and enzymatic preparations used in the authorised oenological practices and processes listed in Annex IV shall meet the requirements of Regulation (EC) No 1332/2008 of the European Parliament and of the Council of 16 December 2008 on food enzymes (*).

(*) OJ L 354, 31.12.2008, p. 7.'

Article 21

Amendments to Directive 2000/13/EC

Directive 2000/13/EC is hereby amended as follows:

1. Article 6(4) shall be amended as follows:

(a) point (a) shall be replaced by the following:

'(a) "Ingredient" shall mean any substance, including additives and enzymes, used in the manufacture or preparation of a foodstuff and still present in the finished product, even if in altered form.';

(b) in point (c)(ii), the introductory word 'additives' shall be replaced by 'additives and enzymes';

(c) in point (c)(iii), the words 'additives or flavouring' shall be replaced by 'additives or enzymes or flavourings';

2. the following indent shall be added to Article 6(6):

'— enzymes other than as referred to in paragraph 4(c)(ii) shall be designated by the name of one of the categories of ingredients listed in Annex II, followed by their specific name,'.

Article 22

Amendments to Directive 2001/112/EC

In Directive 2001/112/EC, in Annex I, Section II(2), the fourth, fifth and sixth indents shall be replaced by the following:

'— Pectolytic enzymes meeting the requirements of Regulation (EC) No 1332/2008 of the European Parliament and of the Council of 16 December 2008 on food enzymes (*);

— Proteolytic enzymes meeting the requirements of Regulation (EC) No 1332/2008;

— Amylolytic enzymes meeting the requirements of Regulation (EC) No 1332/2008.

(*) OJ L 354, 31.12.2008, p. 7.'

Article 23

Amendment to Regulation (EC) No 258/97

In Regulation (EC) No 258/97, the following point shall be added to Article 2(1):

'(d) food enzymes falling within the scope of Regulation (EC) No 1332/2008 of the European Parliament and of the Council of 16 December 2008 on food enzymes (*).

(*) OJ L 354, 31.12.2008, p. 7.'

Article 24

Entry into force

This Regulation shall enter into force on the 20th day following that of its publication in the *Official Journal of the European Union*.

Article 4 shall apply from the date of application of the Community list. Until that date, national provisions in force concerning the placing on the market and use of food enzymes and food produced with food enzymes shall continue to apply in the Member States.

Articles 10 to 13 shall apply from 20 January 2010.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Strasbourg, 16 December 2008.

For the European Parliament
The President
H.-G. PÖTTERING

For the Council
The President
B. LE MAIRE

European Food Safety Authority

The EFSA Journal (2009) 1305, 1-26

SCIENTIFIC OPINION

Guidance of the Scientific Panel of Food Contact Material, Enzymes, Flavourings and Processing Aids (CEF) on the Submission of a Dossier on Food Enzymes for Safety Evaluation by the Scientific Panel of Food Contact Material, Enzymes, Flavourings and Processing Aids [1]

(Question No EFSA-Q-2007-080)

Adopted after public consultation and discussion in the Panel:

23 July 2009

PANEL MEMBERS

Arturo Anadón, David Bell, Mona-Lise Binderup, Wilfried Bursch, Laurence Castle, Riccardo Crebelli, Karl-Heinz Engel, Roland Franz, Nathalie Gontard, Thomas Haertlé, Trine Husøy, Klaus-Dieter Jany, Catherine Leclercq, Jean-Claude Lhuguenot, Wim C. Mennes, Maria Rosaria Milana, Karla Pfaff, Kettil Svensson, Fidel Toldrá, Rosemary Waring, Detlef Wölfle.

[1] For citation purposes: Guidance of EFSA prepared by the Scientific Panel of Food Contact Material, Enzymes, Flavourings and Processing Aids on the Submission of a Dossier on Food Enzymes. *The EFSA Journal* (2009) 1305, 1-26.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

On 16 December 2008 the following Regulations of the European Parliament and of the Council were adopted:

Regulation (EC) No 1332/2008 on food enzymes[2],

Regulation (EC) No 1333/2008 on food additives[3],

Regulation (EC) No 1334/2008 on flavourings and certain food ingredients with flavouring properties[4] and

Regulation (EC) No 1331/2008 on a common authorisation procedure for food additives, food enzymes and food flavourings[5].

The Regulations entered into force on 20 January 2009.

The Regulation (EC) No 1332/2008 on food enzymes applies to enzymes that are added to food to perform a technological function in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food, including enzymes used as processing aids. The scope of this Regulation will therefore not extend to enzymes that are not added to food to perform a technological function but are intended for human consumption, such as enzymes for nutritional purposes. Microbial cultures traditionally used in the production of food, such as cheese and wine, and which may incidentally produce them but are not specifically used to produce them should not be considered food enzymes.

Food enzymes shall be subject to safety evaluation by the European Food Safety Authority (EFSA) and approval via a Community list. The inclusion of a food enzyme in the Community list will be considered by the Commission on the basis of the opinion from EFSA, taking into account also other general criteria such as technological need and consumer aspects. For every food enzyme included in the positive list specifications, including the criteria on purity and the origin of the food enzyme shall be laid down.

Since many food enzymes are already on the market in the Community, the transition to a Community positive list should be smooth and should not lead to unfair conditions for enzyme producers. Therefore, the Regulation provides for an initial period of 24 months, after the date of application of the implementing measures foreseen in the common authorisation procedure in Article 9 of Regulation (EC) No 1331/2008, during which applications can be submitted. The establishment of the Community list will take place in a single step procedure after the Authority has expressed opinions on all food enzymes for which sufficient information has been submitted during the 24-month period.

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[2] OJ L 354, 31.12.2008, p.7
[3] OJ L 354, 31.12.2008, p.16
[4] OJ L 354, 31.12.2008, p.34
[5] OJ L 354, 31.12.2008, p.1

In order to increase consistency in common areas the procedural aspects of approval of food enzymes, as well as for the other two sectoral proposals, such as the handling of applications within well defined deadlines, their evaluation by EFSA and decision making by the Commission, are provided in Regulation (EC) No 1331/2008 on the common authorisation procedure on food additives, food enzymes and food flavourings. This Regulation also provides that implementing measures (Art. 9) shall be adopted by the Commission, within 24 months from the adoption of the Regulation on enzymes, which shall concern in particular the content, drafting and presentation of the application for the evaluation and authorisation of a food enzyme. With a view to the adoption of these implementing measures the Commission consulted the Authority, which, within six months of the date of entry into force of the Regulation on food enzymes, *i.e.* by 20 July 2009 shall present a proposal concerning the data required for risk assessment of the food enzymes.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Article 31 of Regulation (EC) No 178/2002, the European Commission has asked the EFSA to establish guidelines to assist applicants in the preparation and submission of applications for the safety evaluation of food enzymes. In addition, the EFSA has been asked to provide the Commission with a proposal concerning the data required for risk assessment of food enzymes with a view to including it in the implementing measures which will lay down amongst other aspects, the content, drafting and presentation of an application for the evaluation and authorisation of food enzymes.

ACKNOWLEDGEMENTS

The European Food Safety Authority wishes to thank the members of the Working Group for the preparation of this guidance document: A. Anadón, D. Bell, T. Haertlé, T. Hallas-Møller, K.-D. Jany, P. Joudrier, P. Tobback, F. Toldrá, R. Waring and A. Pöting for assisting in the preparation of the draft guidance document under the AFC Panel mandate.

INTRODUCTION

The purpose of this document is to provide guidance to applicants and other interested parties in providing a dossier for safety evaluation accordance with Regulation (EC) No 1332/2008 on food enzymes. It gives guidance on the format (hereafter referred to as a "dossier") of a formal application for the safety assessment of a food enzyme, on the administrative and technical data required, and on the range of toxicological tests generally required. The application is initially made to the European Commission, for further transmission to the European Food Safety Authority, which is responsible for carrying out the safety assessment and providing an opinion on the outcome of the evaluation. All the information necessary to enable EFSA to conduct a safety assessment of a food enzyme must be provided by the applicants in the dossier.

General Principles of Risk Assessment of Food Enzymes

In order to enable EFSA to carry out the safety assessment, the following critical issues of risk assessment are:

- **The source**[6]. A consideration of safety issues related to the source of the food enzyme (animals, plants, basidiomycetes or micro-organisms). The possibility of infectious agents in the source, measures for their control in the food enzyme and the potential virulence / toxicity of the producer organism/micro-organism have to be considered.
- **The food enzyme**, related to the enzyme protein(s) as well as other constituents, *e.g.* by-products originating from the source organism and residues of any substances and materials used in the production process.
- **Intended and unintended reaction products** resulting either from enzymatic or chemical reactions of the food enzyme with food constituents or from the degradation of the food enzyme during storage and processing of the foodstuff.
- **The dietary exposure of the consumer.** This depends on the residual concentration of the food enzyme(s) and other constituents of the food enzyme in the foods at the time of consumption and the amount and frequency of their consumption.

Each individual food enzyme must be assessed. However, specified food enzymes

i) with the same catalytic activity (*e.g.* alpha-amylase) and,

ii) produced by the same micro-organism strain and

iii) by the substantially same manufacturing process as described in section 3.2.2, may be grouped in one application.

The guidance document is based on the "Guidelines for the presentation of data on food enzymes of the Scientific Committee for Food (SCF)" (SCF, 1992), taking into account the recommendations of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) (FAO/WHO, 2006) and national authorities or advisory committees of EU Member States (Agence Française de Sécurité Sanitaire des Aliments (AFSSA) (AFSSA, 2003), Danish Veterinary and Food Administration (DVFA) (DVFA, 2005), UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) (Battershill,1993).

[6] A food enzyme contains an active enzyme (in some instances a blend of two or more enzymes). Furthermore it may also contain constituents of the source organism (*i.e.* an animal, plant, or microbial material from which an enzyme was isolated) and compounds derived from the manufacturing process, for example, the residues of the fermentation broth.

SCOPE

The scope of this guidance document is confined to the safety evaluation of food enzymes falling within the scope of Regulation (EC) No 1332/2008 on food enzymes (Article 3, Definitions).

"Food enzyme" means a product obtained from plants, animals or micro-organisms or products thereof including a product obtained by a fermentation process using micro-organisms:

i. containing one or more enzymes capable of catalysing a specific biochemical reaction; and

ii. added to food for a technological purpose at any stage of manufacturing, processing, preparation, treatment, packaging, transport or storage of foods.

"Food enzyme preparation" means a formulation consisting of one or more food enzymes in which substances such as food additives and/or other food ingredients are incorporated to facilitate their storage, sale, standardisation, dilution or dissolution.

This guidance document is not intended to be exhaustive, since information requirements are likely to vary depending on the food enzyme's function/activity, the properties of the source material, the properties and amounts of any by-products and substances originating from the production process, the history of previous consumption as well as the intended use and the resulting level of human dietary exposure. There may be circumstances where additional data or tests are required for the evaluation of the safety in use. On the other hand, if some of the data stipulated in the guidance document are considered irrelevant, they may be omitted provided that the safety assessment can be adequately addressed. Additionally, progress in science and technology may necessitate periodic updating of this guidance document to reflect new information requirements.

This guidance document does not cover risk assessment for user/worker safety.

SUBMISSION OF AN APPLICATION

Applications shall be submitted in accordance with Regulation (EC) 1331/2008 and its implementing measures referred to in Article 9 of this Regulation. The applicant shall provide all available data relevant for the evaluation by EFSA. For the purposes of the current guidance, the definitions laid down in the Regulation (EC) 1332/2008 on food enzymes shall apply (s. Appendix).

Applicants should note that the Commission will make available to competent authorities in Member States in full form any dossier submitted to the Authority for a safety assessment (Art. 4 of the Regulation (EC) No 1331/2008). Confidentiality of information provided by the applicant will be treated in accordance with Article 12 of the Regulation (EC) No 1331/2008. Therefore applicants should mark clearly which of the information provided they wish to be treated as confidential and provide verifiable justification in such case.

The applicant should submit a dossier with the full information, both on paper and in electronic format on a standard physical media (*e.g.* CD ROM). It has to be declared by letter that the electronic and the paper versions are identical.

In addition to the complete version with the full information, applicants are requested to provide a second version of the CD ROM without the confidential information. This version will be made available to anyone who might submit a request for access to documents to EFSA.

Any specific literature reference (such as scientific papers) mentioned and used to support the petition must be supplied in the dossier as full length paper. When reference is made to a book or to extensive publications, only the relevant parts need be supplied.

Applicants may deviate from the guidance, provided valid and documented scientific reasons are given in the dossier. In all cases EFSA may request additional data.

INFORMATION TO BE SUPPLIED WITH AN APPLICATION FOR A FOOD ENZYME

In order for EFSA to carry out a safety evaluation of a food enzyme, applicants and other interested parties wishing to introduce food enzymes into the EU market according to Regulation (EC) No 1332/2008 on food enzymes should include the following information when submitting a dossier[7]:

[7] Dossiers are initially submitted to the European Commission for onward transmission to EFSA, and may be made available to outside parties. Applicants should therefore indicate if any parts of the dossier are confidential business information in accordance to the legislation provisions. Applicants are requested to retain copies of their petition.

Title of the dossier (including food enzyme name and food enzyme source)

i. Summary of Dossier Submission
ii. Administrative Data
iii. Technical Data
iv. Toxicological Data
v. Conclusion
vi. Bibliography, References (original papers) and Reports

1. Summary of Dossier Submission

A summary of the data which has been submitted by any interested party or parties in support of a food enzyme should be provided at the start of the dossier. The summary should follow the same order as described for the main dossier and include the following information:

i. Identity of the Food Enzyme
ii. Chemical Composition and Properties of the Food Enzyme
iii. Source materials and Manufacturing Process
iv. Reaction and Fate in Foods
v. Proposed Uses in specific Food Products or Food Categories
vi. Main Findings of Toxicological Tests

Applicants should also present their own conclusions as to the likely safety-in-use of the food enzyme, drawing attention to any unusual features in the data presented.

The summary should not contain any confidential information as it will be made available to the public on request.

2. Administrative Data

A dossier on a food enzyme for safety evaluation by EFSA should include information on the following:

i. Name, address and other contact details of the applicant(s), and/or other interested parties *(e.g.* company, organisation, *etc.*) to include telephone number(s), fax number(s), email(s)
ii. Name, address and other contact details of the manufacturer(s) of the food enzyme (if different from above) to include telephone number(s), fax number(s), email(s)
iii. Name, address and other contact details (if different from above) of the person(s) responsible for the dossier
iv. Date of submission of the dossier
v. Scope of the application (*e.g.* new food enzyme or previously evaluated food enzyme produced by new production methods, new starting materials, extension of use)
vi. If relevant reference to any similar food enzyme(s) already evaluated/authorised on the market within the EU or internationally
vii. A table of contents for the submitted dossier

3. Technical Data

In this section, the food enzyme should be characterised as completely as possible. The following information should be included and submitted as part of the dossier:

3.1 Identity of the Food Enzyme

The identity and the properties of the food enzyme should be described as completely as possible. The food enzyme sample tested toxicologically should be representative of the food enzyme to be authorised for use in food processing *(*s. Section 4 of the guidance*)*. This should be stated explicitly in the dossier. If the samples are not representative of the commercial product then a justification should be provided. The following paragraphs list the general requirements of dossier submissions to establish the identity of a food enzyme.

3.1.1 Name(s), Synonyms, Abbreviations and Classification(s)

i. Common Name(s) and/or Trade Name(s) *(if applicable)*
ii. Enzyme Classification Number of Enzyme Commission of the International Union of Biochemistry and Molecular Biology (IUBMB) [8] *(if applicable)*
iii. Chemical Name(s) *(if applicable)*
iv. Chemical Abstract Service (CAS) Registry Number *(if available)*
v. European Inventory of Existing Chemical Substances Number (EINECS) or European List of Notified Chemical Substances Number *(*ELINCS*)* *(if available)*

3.1.2 Chemical Composition and Properties of the Food Enzyme

3.1.2.1 Chemical Composition

The following should be provided:

i. Molecular mass of the food enzyme and subunit structure; and amino acid sequence (if available),
ii. Chemical description of the food enzyme as tested including chemical purity and identity and percentage or concentration of chemical impurities originating from the source and/or the production process (*e.g.* metabolites such as mycotoxins, heavy metals, residues of extraction solvents) and the methods of analysis,
iii. Information on whether the food enzyme is modified by post translational process or by technological procedures,
iv. Information on whether the food enzyme is protein engineered, the nature of the modification and the rational for the modification, *e.g.* enhancing pH or thermal stability,
v. Data on the batch-to-batch variability for the relevant parameters,
vi. Data on the reproducibility for relevant parameters.

[8] The IUBMB was formerly the International Union of Biochemistry. The IUBMB assigns each enzyme a recommended name and a 4-part distinguishing number and divides enzymes into six main groups: Oxidoreductases, Transferases, Hydrolases, Lyases, Isomerases and Ligases

vii. Any other useful information such as the concentration of the Total Organic Solids (TOS) as defined by JECFA (FAO/WHO, 2006)

3.1.2.2 Proposed Chemical and Microbiological Specification

The proposed specifications should be submitted in a format modelled on recent EU or other internationally accepted specifications. Where the proposed specifications differ from any already existing JECFA or other internationally recognised specification, these specifications should be set out alongside the proposed new specification, and any differences pointed out.

Other data which the applicant considers useful in describing the composition of a food enzyme should also be supplied.

3.1.2.3 Properties of the Food Enzyme

The following should be provided:

i. Information on the principal enzymatic activity, specifying substrates, reaction products and required co-factors. Measurement of the activity should be based on a reference method using a standard substrate. Details of the activity should be given in enzyme activity units (U) per unit weight (specific activity) or by the SI unit (Katal (kat =· mol · s^{-1}) [9]). The enzyme assay method and methods for determination of principal and side reactions, along with information on the stability of the food enzyme during food processing/storage should be provided.

ii. The activity of the food enzyme under the conditions of the intended use and the influence of reaction conditions (*e.g.* the optimum pH and temperature, as well as inhibitors, activating compounds and co-factors),

iii. Any subsidiary/side activities should be characterised, if possible and where appropriate. In particular those activities should be specified that might cause adverse effects (*e.g.* protease and phospholipase activities due to their action on the mucous membranes) and/or form toxic metabolites,

iv. Data on the stability of the food enzyme during storage and before use.

[9] The amount of food enzyme present or used in food production can be difficult to determine in absolute terms such as grams. However, parameters such as the activity of the food enzyme or food enzyme preparation used in production are more relevant. The activity is typically measured by an enzyme activity unit (U) which is the amount of enzyme which will catalyse the transformation of one micromole of the substrate per minute under standard conditions (IUPAC, 1974). The SI Unit of activity *(i.e.* enzyme activity*)* is the Katal (kat = mol · s^{-1}·) which was proposed as a replacement for the enzyme activity unit (U) in 1978. It is a derived SI unit for expressing quantity values of activity of enzymes and other catalysts. However, in practice, enzyme activity units are still more commonly used than the Katal.

3.2 Source Materials and Manufacturing Process

3.2.1 Source Materials

Food enzymes are produced from animal, plant, basidiomycete and microbial sources. Note that microbial sources include prokaryotes, protozoa, microalgae, and all fungi (including moulds, yeasts and filamentous fungi), but that fungal basidiomycete fruiting bodies/mycelia are considered together with plant sources. The specific information which should be included and submitted as part of the dossier in the case of animal, plant and basidomycete and microbial sources is outlined below.

The most recent taxonomic classification and identification methods used in determining the classification should be provided including genus, species, sub-species (if appropriate). In the case of micro-organisms and fungi, applicants are recommended to refer to the Organisation for Economic Cooperation and Development (OECD) Guidance Document on the use of Taxonomy in Risk Assessment of Micro-organisms: Bacteria (OECD, 2003).

3.2.1.1 Production from Animal Sources

i. Information should be provided on which animal tissue is used for production as well as history of previous consumption of the tissue in question, in particular on whether there is a documented history of use with absence of human health adverse effects. Information should also be provided as to whether the animal tissue is fit for human consumption or derives from a Cat. 3 Animal By-Product according to Regulation (EC) 1774/2002 as amended.

ii. Information should be provided as to whether animal tissues used for the preparation of food enzymes comply with meat inspection requirements and are handled in accordance with good hygienic practice; if not, justification should be given.

iii. Information should be provided on methods used to ensure the absence of any risk of infectivity (*e.g.* the agent of transmissible spongiform encephalopathies (TSEs), parasites or other zoonotic agents).

iv. Data on non-infectivity should be supplied based on the classification of the tissues in terms of their infectious titre in natural diseases established by the WHO (WHO, 2003).

3.2.1.2 Production from Plant and Basidiomycete Sources

i. The part(s) of the plant or basidiomycete fruiting bodies/mycelia used for the production of the food enzyme should be specified.

ii. Information should be provided on previous consumption, in particular on whether there is a documented history of safe use.

iii. Relevant information should be provided on methods used for ensuring absence of substances that might cause adverse health effects to humans. For any residue of such

substances remaining in the food enzyme, the name and amount should be specified in section 3.1.2.1 and limits should be proposed in section 3.1.2.2.

iv. If a genetically modified plant or fungus is used, information should also be provided on the organism in accordance with the Guidance document of the Scientific Panel on Genetically Modified Organisms for the Risk Assessment of Genetically Modified Plants and Derived Food and Feed (EFSA, 2006a). If the source is already covered by an authorisation in accordance with Regulation (EC) No 1829/2003[10] on genetically modified food and feed[11], information concerning the risk assessment and authorisation of the GMO should be provided.

3.2.1.3 Production from Microbial Sources

Although neither pathogenic or toxigenic micro-organisms are intentionally used in the production of food enzymes, individual strains of certain microbial fungal species traditionally used as sources of food enzymes may produce toxic secondary metabolites under certain fermentation conditions conducive to the production of these compounds. Some of these micro-organisms are now used as sources of recombinantly expressed enzymes (Olempska-Beer *et al.*, 2006). The key component of evaluating food enzyme safety from microbial sources is the safety assessment of the production strain, in particular, its pathogenic and toxigenic potential (Pariza and Johnson, 2001). In the case of food enzymes produced by fermentation processes using micro-organisms, the following information on the micro-organism is required:

i. Information about the strain used for food enzyme production

- The taxonomic identity of the strain must be provided.
- Details of any documented history of use with absence of human health adverse effects including Qualified Presumption of Safety (QPS) (EFSA, 2005) status should be provided if available.

ii. For genetically modified micro-organisms (GMM), the presence of any factor(s) affecting the genetic stability of the producer strain

Additional information should be provided according to the `Guidance Document of the Scientific Panel on Genetically Modified Organisms for the Risk Assessment of Genetically Modified Micro-organisms and their Derived Products Intended for Food and Feed Use` (EFSA, 2006b).

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[10] OJ L 268, 18.10.2003, p. 1